	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	941	(glucagon-like adj peptide) or glp-1 or glp-2	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:28			0
2	BRS	L2	2433	lipophilic adj (substituent or group)	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:39			0
3	BRS	L3	39	((glucagon-like adj peptide) or glp-1 or glp-2) same (lipophilic adj (substituent or group))	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:39			0
4	BRS	L4	15372	(fatty adj acid) same (amino)	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:46			0
5	BRS	L5	12	1 same 4	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:47			0
6	BRS	L6	470	spacer same ((succinic adj acid) or glu or asp)	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:49			0
7	BRS	L7	7	3 same 6	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 13:49			0
8	BRS	L8	1397	tetradecanoyl	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 14:09			0
9	BRS	L9	23	1 same 8	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 14:10			0
10	BRS	L10	4	1 same 8 same 2	USPAT; US-PGPUB; EPO; DERWENT	2003/06/26 14:10			0
11	BRS	L11	20	jonassen adj ib.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/26 14:10			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
12	BRS	L12	35	havelund adj svend.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/26 14:11			0
13	BRS	L13	5	halstrom adj john.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/26 14:11			0
14	BRS	L14	5	hansen adj per adj hertz.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/26 14:12			0
15	BRS	L15	4	((jonassen adj ib.in.) or (havelund adj svend.in.) or (hansen adj per adj hertz.in.) or (halstrom adj john.in.)) and ((glucagon-like adj peptide) or glp-1 or glp-2)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/26 14:12			0

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=> file medline caplus biosis emb    scisearch agricola
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.21       0.21

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FILE 'SCISEARCH' ENTERED AT 14:18:34 ON 26 JUN 2003
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FILE 'AGRICOLA' ENTERED AT 14:18:34 ON 26 JUN 2003

=> s (glucagon-like peptide-1) or (glucagon-like peptide-2) or glp-1 or glp-2
L1        9755 (GLUCAGON-LIKE PEPTIDE-1) OR (GLUCAGON-LIKE PEPTIDE-2) OR GLP-1
               OR GLP-2

=> s lipophilic (w) (substituent or group)
L2        1577 LIPOPHILIC (W) (SUBSTITUENT OR GROUP)

=> s l1 (p) l2
L3           8 L1 (P) L2

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L3
L4           7 DUPLICATE REMOVE L3 (1 DUPLICATE REMOVED)

=> d l4 1-7 ibib abs

L4   ANSWER 1 OF 7  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   2002:609774  BIOSIS
DOCUMENT NUMBER:    PREV200200609774
TITLE:              Derivatives of GLP-1 analogs.
AUTHOR(S):          Knudsen, Liselotte Bjerre (1); Huusfeldt, Per Olaf;
                    Nielsen, Per Franklin
CORPORATE SOURCE:   (1) Valby Denmark
                    ASSIGNEE: Novo Nordisk A/S, Bagsvaerd, Denmark
PATENT INFORMATION: US 6458924 October 01, 2002
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (Oct. 1, 2002) Vol. 1263, No. 1, pp. No
                    Pagination. http://www.uspto.gov/web/menu/patdata.html.
                    e-file.
                    ISSN: 0098-1133.
DOCUMENT TYPE:      Patent
LANGUAGE:           English
AB   The present invention relates to a pharmaceutical composition comprising a
       ***GLP***  -  ***1***  derivative having a  ***lipophilic***
       ***substituent***  ; and a surfactant.

L4   ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2003 ACS         DUPLICATE 1
ACCESSION NUMBER:        2001:721487  CAPLUS
DOCUMENT NUMBER:         135:273221
TITLE:                   Preparation of lipophilic human glucagon-like
                         peptide-1 derivatives with protracted action profiles
INVENTOR(S):             Knudsen, Liselotte; Huusfeldt, Per Olaf; Nielsen, Per
                         Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk;
                         Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl;
                         Madsen, Kjeld
PATENT ASSIGNEE(S):      Novo Nordisk A/s, Den.
SOURCE:                  U.S., 136 pp., Cont.-in-part of U.S. Ser. No. 38,432,
                         abandoned.
                         CODEN: USXXAM
DOCUMENT TYPE:           Patent
LANGUAGE:                English
```

FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6268343	B1	20010731	US 1999-258750	19990226
WO 9808871	A1	19980305	WO 1997-DK340	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001011095	A2	20010116	JP 2000-152778	19970822
ZA 9901571	A	19990902	ZA 1999-1571	19990226
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
US 2002025933	A1	20020228	US 2001-908534	20010718

PRIORITY APPLN. INFO.:

DK 1996-931	A	19960830
DK 1996-1259	A	19961108
DK 1996-1470	A	19961220
US 1997-36255P	P	19970124
US 1997-36226P	P	19970125
WO 1997-DK340	A2	19970822
US 1997-918810	B2	19970826
DK 1998-263	A	19980227
DK 1998-264	A	19980227
DK 1998-268	A	19980227
DK 1998-272	A	19980227
DK 1998-274	A	19980227
US 1998-38432	B2	19980311
DK 1998-508	A	19980408
DK 1998-509	A	19980408
US 1998-82478P	P	19980421
US 1998-82480P	P	19980421
US 1998-84357P	P	19980421
US 1998-82802P	P	19980423
US 1997-35905P	P	19970124
JP 1998-511183	A3	19970822
US 1997-922200	B2	19970902
DK 1998-271	A	19980227
US 1998-78422P	P	19980318
US 1998-82479P	P	19980421
US 1998-85789P	P	19980518
US 1999-258187	B1	19990225
US 1999-258750	A2	19990226
US 1999-265141	A2	19990308

OTHER SOURCE(S): MARPAT 135:273221

AB The present invention relates to human ***glucagon*** - ***like*** ***peptide*** - ***1*** (***GLP*** - ***1***) derivs. having a ***lipophilic*** ***substituent*** , compns. contg. these derivs., and to methods for their prepn. A claimed compd. is His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly. Thus, coupling of ***GLP*** - ***1*** (7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (prepn. given), followed by deesterification with CF3CO2H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH2)12CO-.gamma.-Glu]26,34- ***GLP*** - ***1*** (7-37)-OH. Several prepd. lipophilic ***GLP*** - ***1*** analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than ***GLP*** - ***1*** (7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic ***GLP*** - ***1*** deriv. selected. The efficacy of several prepd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human ***GLP*** - ***1*** receptor.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:566665 CAPLUS
DOCUMENT NUMBER: 135:122756
TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen,

	Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdal; Madsen, Kjeld
PATENT ASSIGNEE(S):	Den.
SOURCE:	U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 265,141. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
WO 9808871	A1	19980305	WO 1997-DK340	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001011095	A2	20010116	JP 2000-152778	19970822
US 6268343	B1	20010731	US 1999-258750	19990226
US 6384016	B1	20020507	US 1999-265141	19990308
US 2002025933	A1	20020228	US 2001-908534	20010718

PRIORITY APPLN. INFO.:	DK 1996-931	A	19960830
	DK 1996-1259	A	19961108
	DK 1996-1470	A	19961220
	US 1997-36255P	P	19970124
	US 1997-36226P	P	19970125
	US 1998-84357P	P	19970822
	WO 1997-DK340	W	19970822
	US 1997-918810	B2	19970826
	DK 1998-263	A	19980227
	DK 1998-264	A	19980227
	DK 1998-268	A	19980227
	US 1998-38432	B2	19980311
	US 1998-78422P	P	19980318
	US 1998-82478P	P	19980421
	US 1998-82479P	P	19980421
	US 1998-82480P	P	19980421
	US 1998-82802P	P	19980423
	US 1999-258750	A2	19990226
	US 1999-265141	A2	19990308
	US 1997-35905P	P	19970124
	JP 1998-511183	A3	19970822
	US 1997-922200	B2	19970902
	DK 1998-271	A	19980227
	DK 1998-272	A	19980227
	DK 1998-274	A	19980227
	EP 1998-610006	A	19980313
	DK 1998-508	A	19980408
	DK 1998-509	A	19980408
	US 1998-85789P	P	19980518
	US 1999-258187	B1	19990225

OTHER SOURCE(S): MARPAT 135:122756

AB The present invention relates to pharmaceutical compns. comprising lipophilic human ***glucagon*** - ***like*** ***peptide*** - ***1*** (***GLP*** - ***1***) derivs. having a ***lipophilic*** ***substituent*** and a surfactant. Thus, coupling of ***GLP*** - ***1*** (7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (prepn. given), followed by deesterification with CF3CO2H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH2)12CO-.gamma.-Glu]26,34- ***GLP*** - ***1*** (7-37)-OH. Several prepd. lipophilic ***GLP*** - ***1*** analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than ***GLP*** - ***1*** (7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic ***GLP*** - ***1*** deriv. selected. The efficacy of several prepd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human ***GLP*** - ***1*** receptor.

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:566077 CAPLUS

DOCUMENT NUMBER: 131:194808
TITLE: GLP-1 de[redacted]atives of GLP-1 and exendin wi[redacted]a protracted profile of action
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Madsen, Kjeld
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943708	A1	19990902	WO 1999-DK86	19990225
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9932477	A1	19990915	AU 1999-32477	19990225
EP 1056775	A1	20001206	EP 1999-936077	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
ZA 9901571	A	19990902	ZA 1999-1571	19990226
US 2001047084	A1	20011129	US 2001-886311	20010621

PRIORITY APPLN. INFO.:
DK 1998-274 A 19980227
US 1998-84357P P 19980505
WO 1999-DK86 W 19990225
US 1999-312177 B1 19990514

AB The present invention relates to derivs. exendin and of ***GLP*** - ***1*** (7-C), wherein C is 35 or 36, which derivs. have just one ***lipophilic*** ***substituent*** which is attached to the C-terminal amino acid residue. The derivs. have a protracted action relative to ***GLP*** - ***1*** (7-37) and are useful for treating insulin-dependent and noninsulin-dependent diabetes mellitus. The derivs. of the invention can be combined with other antidiabetics or oral hypoglycemic agents. Pharmaceutical formulations contg. the derivs. of the invention are also claimed.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:566075 CAPLUS
DOCUMENT NUMBER: 131:200093
TITLE: Preparation of GLP-1 analogs for treatment of obesity and non-insulin dependent diabetes mellitus
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Pedersen, Freddy Zimmerdahl
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943706	A1	19990902	WO 1999-DK82	19990225
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926106	A1	19990915	AU 1999-26106	19990225
EP 1060191	A1	20001220	EP 1999-906076	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, FI, RO				
ZA 9901569	A	19990827	ZA 1999-1569	19990226

ZA 9901570 A 19990902 ZA 1999-1570 19990226
PRIORITY APPLN. INFO.: DK 1998-268 A 19980[redacted]
WO 1999-DK82 W 19990[redacted]
OTHER SOURCE(S): MARPAT 131:200093
AB ***GLP*** - ***1*** analog derivs. His-Xaa8-Xaa9-Gly-Xaa11-Phe-Thr-Xaa14-Asp-Xaa16-Xaa17-Xaa18-Xaa19-Xaa20-Xaa21-Xaa22-Xaa23-Xaa24-Xaa25-Xaa26-Xaa27-Phe-Ile-Xaa30-Xaa31-Xaa32-Xaa33-Xaa34-Xaa35-Xaa36-Xaa37-Xaa38-Xaa39-Xaa40-Xaa41-Xaa42-Xaa43-Xaa44-Xaa45 [Xaa represents an amino acid residue, e.g., Xaa8, Xaa25, Xaa30 = Ala, Gly, Ser, Thr, Leu, Ile, Val, Glu, Asp, Lys; Xaa9, Xaa21, Xaa27 = Glu, Asp, Lys; Xaa11 = Thr, Ala, Gly, Ser, Leu, Ile, Val, Glu, Asp, Lys; Xaa14, Xaa17, Xaa18 = Val, Ala, Gly, Ser, Thr, Leu, Ile, Tyr, Glu, Asp, Lys] having a ***lipophilic*** ***substituent*** were prepd. for the treatment of obesity and non-insulin dependent diabetes mellitus. Thus, Arg26-34,Lys36[N.epsilon.-[.gamma.-glutamyl(N.alpha.-hexadecanoyl)]] ***GLP*** - ***1*** (7-36)-OH was prepd. via reaction of Arg26-34,Lys36 ***GLP*** - ***1*** (7-36)-OH with Pal-Glu(ONSu)-But (Pal = hexadecanoyl, NSU = succinimide residue). The synthesized compds. have a protracted profile of action relative to ***GLP*** - ***1*** (7-37).
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:566074 CAPLUS
DOCUMENT NUMBER: 131:194807
TITLE: Insulinotropic N-terminally truncated GLP-1 lipophilic derivatives with protracted action
INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943705	A1	19990902	WO 1999-DK81	19990225
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926105	A1	19990915	AU 1999-26105	19990225
EP 1056774	A1	20001206	EP 1999-906075	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002508162	T2	20020319	JP 2000-533455	19990225

PRIORITY APPLN. INFO.: DK 1998-264 A 19980227
DK 1998-509 A 19980408
WO 1999-DK81 W 19990225
OTHER SOURCE(S): MARPAT 131:194807
AB The present invention relates to N-terminally truncated derivs. of human ***glucagon*** - ***like*** ***peptide*** - ***1*** (***GLP*** - ***1***) and analogs thereof having a protracted profile of action, as well as the use of such derivs. in pharmaceutical compns. for the treatment of obesity, insulin dependent or non-insulin dependent diabetes mellitus. The ***GLP*** - ***1*** derivs. have a ***lipophilic*** ***substituent*** attached to at least one amino acid residue.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:163616 CAPLUS
DOCUMENT NUMBER: 128:244341
TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles
INVENTOR(S): Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808871	A1	19980305	WO 1997-DK340	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738478	A1	19980319	AU 1997-38478	19970822
AU 732957	B2	20010503		
EP 944648	A1	19990929	EP 1997-935509	19970822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
CN 1232470	A	19991020	CN 1997-198413	19970822
BR 9711437	A	20000118	BR 1997-11437	19970822
JP 2000500505	T2	20000118	JP 1998-511183	19970822
JP 3149958	B2	20010326		
JP 2001011095	A2	20010116	JP 2000-152778	19970822
NO 9900950	A	19990428	NO 1999-950	19990226
US 6268343	B1	20010731	US 1999-258750	19990226
KR 2000035964	A	20000626	KR 1999-701750	19990302
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
US 2002025933	A1	20020228	US 2001-908534	20010718

PRIORITY APPLN. INFO.:

DK 1996-931	A	19960830
DK 1996-1259	A	19961108
DK 1996-1470	A	19961220
US 1997-35905P	P	19970124
US 1997-36255P	P	19970124
US 1997-36226P	P	19970125
JP 1998-511183	A3	19970822
WO 1997-DK340	W	19970822
US 1997-918810	B2	19970826
US 1997-922200	B2	19970902
DK 1998-263	A	19980227
DK 1998-264	A	19980227
DK 1998-268	A	19980227
DK 1998-271	A	19980227
DK 1998-272	A	19980227
DK 1998-274	A	19980227
US 1998-38432	B2	19980311
US 1998-78422P	P	19980318
DK 1998-508	A	19980408
DK 1998-509	A	19980408
US 1998-82478P	P	19980421
US 1998-82479P	P	19980421
US 1998-82480P	P	19980421
US 1998-84357P	P	19980421
US 1998-82802P	P	19980423
US 1998-85789P	P	19980518
US 1999-258187	B1	19990225
US 1999-258750	A2	19990226
US 1999-265141	A2	19990308

AB Lipophilic human ***glucagon*** - ***like*** ***peptide*** - ***1*** (***GLP*** - ***1***) derivs. and analogs thereof having a ***lipophilic*** ***substituent*** have interesting pharmacol. properties, in particular they have a more protracted profile of action than ***GLP*** - ***1*** (7-37). Thus, coupling of ***GLP*** - ***1*** (7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (prepn. given), followed by deesterification with CF3CO2H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH2)12CO-.gamma.-Glu]26,34- ***GLP*** - ***1*** (7-37)-OH (NNC 90-1167). Several prepd. lipophilic ***GLP*** - ***1*** analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than ***GLP*** - ***1*** (7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic ***GLP*** - ***1*** deriv. selected. The efficacy of several prepd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human ***GLP*** - ***1*** receptor.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s (fatty acid) (p) amino
L5       30193 (FATTY ACID) (P) AMINO

=> d his

     (FILE 'HOME' ENTERED AT 14:18:05 ON 26 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     14:18:34 ON 26 JUN 2003
L1          9755 S (GLUCAGON-LIKE PEPTIDE-1) OR (GLUCAGON-LIKE PEPTIDE-2) OR GLP
L2          1577 S LIPOPHILIC (W) (SUBSTITUENT OR GROUP)
L3             8 S L1 (P) L2
L4             7 DUPLICATE REMOVE L3 (1 DUPLICATE REMOVED)
L5         30193 S (FATTY ACID) (P) AMINO

=> s l1 (p) l5
L6            21 L1 (P) L5

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L6
L7            10 DUPLICATE REMOVE L6 (11 DUPLICATES REMOVED)

=> s l7 not l4
L8            10 L7 NOT L4

=> s l8 (p) substit?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L40 (P) SUBSTIT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L43 (P) SUBSTIT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L46 (P) SUBSTIT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L49 (P) SUBSTIT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L52 (P) SUBSTIT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L55 (P) SUBSTIT?'
L9             2 L8 (P) SUBSTIT?

=> d l10 1-2 ibib abs
L10 NOT FOUND
The L-number entered has not been defined in this session, or it
has been deleted.  To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d l8 1-2 ibib abs

L8   ANSWER 1 OF 10     MEDLINE
ACCESSION NUMBER:    2000256912     MEDLINE
DOCUMENT NUMBER:     20256912   PubMed ID: 10794683
TITLE:               Potent derivatives of glucagon-like peptide-1 with
                     pharmacokinetic properties suitable for once daily
                     administration.
AUTHOR:              Knudsen L B; Nielsen P F; Huusfeldt P O; Johansen N L;
                     Madsen K; Pedersen F Z; Thogersen H; Wilken M; Agerso H
CORPORATE SOURCE:    Department of Molecular Pharmacology, Health Care Discovery
                     and Preclinical Development, Novo Nordisk A/S, Novo Park,
                     DK-2760 Maaloev, Denmark.. lbkn@novo.dk
SOURCE:              JOURNAL OF MEDICINAL CHEMISTRY, (2000 May 4) 43 (9) 1664-9.
                     Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200006
ENTRY DATE:          Entered STN: 20000706
                     Last Updated on STN: 20000706
                     Entered Medline: 20000629
AB   A series of very potent derivatives of the 30-  ***amino***   acid peptide
     hormone   ***glucagon***  -  ***like***    ***peptide***  -  ***1***   (
       ***GLP***  -  ***1***  ) is described.  The compounds were all derivatized
```

with ***fatty*** ***acids*** in order to protract their action by facilitating binding to serum albumin. ***GLP*** - ***1*** had a potency (EC(50)) of 55 pM for the cloned human ***GLP*** - ***1*** receptor. Many of the compounds had similar or even higher potencies, despite quite large substituents. All compounds derivatized with ***fatty*** ***acids*** equal to or longer than 12 carbon atoms were very protracted compared to ***GLP*** - ***1*** and thus seem suitable for once daily administration to type 2 diabetic patients. A structure-activity relationship was obtained. ***GLP*** - ***1*** could be derivatized with linear ***fatty*** ***acids*** up to the length of 16 carbon atoms, sometimes longer, almost anywhere in the C-terminal part without considerable loss of potency. Derivatization with two ***fatty*** ***acid*** substituents led to a considerable loss of potency. A structure-activity relationship on derivatization of specific ***amino*** acids generally was obtained. It was found that the longer the ***fatty*** ***acid*** , the more potency was lost. Simultaneous modification of the N-terminus (in order to obtain better metabolic stability) interfered with ***fatty*** ***acid*** derivatization and led to loss of potency.

L8 ANSWER 2 OF 10 MEDLINE
ACCESSION NUMBER: 95363369 MEDLINE
DOCUMENT NUMBER: 95363369 PubMed ID: 7636436
TITLE: Luminal glucagon-like peptide-1(7-36) amide-releasing factors in the isolated vascularly perfused rat colon.
AUTHOR: Plaisancie P; Dumoulin V; Chayvialle J A; Cuber J C
CORPORATE SOURCE: INSERM Unite 45, Pavillon H bis, Hopital Edouard Herriot, Lyon, France.
SOURCE: JOURNAL OF ENDOCRINOLOGY, (1995 Jun) 145 (3) 521-6. Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 19950921
Entered Medline: 19950913

AB ***Glucagon*** - ***like*** ***peptide*** - ***1*** (***GLP*** - ***1***) is released from endocrine cells of the distal part of the gut after ingestion of a meal. ***GLP*** - ***1*** secretion is, in part, under the control of hormonal and/or neural mechanisms. However, stimulation of the colonic L cells may also occur directly by the luminal contents. This was examined in the present study, using an isolated vascularly perfused rat colon. ***GLP*** - ***1*** immunoreactivity was measured in the portal effluent after luminal infusion of a variety of compounds which are found in colonic contents (nutrients, fibers, bile acids, short-chain ***fatty*** ***acids*** (SCFAs)). Oleic acid (100 mM) or a mixture of ***amino*** acids (total concentration 250 mM), or starch (0.5%, w/v) did not increase ***GLP*** - ***1*** secretion over basal value. A pharmacological concentration of glucose (250 mM) elicited a marked release of ***GLP*** - ***1*** which was maximal at the end of infusion (400% of basal), while 5 mM glucose was without effect on secretion. Pectin evoked a dose-dependent release of ***GLP*** - ***1*** over the range 0.1-0.5% (w/v) with a maximal response at 360% of basal when 0.5% pectin was infused. Cellulose or gum arabic (0.5%) did not modify ***GLP*** - ***1*** secretion. The SCFAs acetate, propionate or butyrate (5, 20 and 100 mM) did not induce a significant release of ***GLP*** - ***1*** . Among the four bile acids tested, namely taurocholate, cholate, deoxycholate and hyodeoxycholate, the last one was the most potent at eliciting a ***GLP*** - ***1*** response with a maximal release at 300% and 400% of the basal value when 2 and 20 mM bile acid were administered respectively.(ABSTRACT TRUNCATED AT 250 WORDS)

=> d his

(FILE 'HOME' ENTERED AT 14:18:05 ON 26 JUN 2003)

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L1 9755 S (GLUCAGON-LIKE PEPTIDE-1) OR (GLUCAGON-LIKE PEPTIDE-2) OR GLP
L2 1577 S LIPOPHILIC (W) (SUBSTITUENT OR GROUP)
L3 8 S L1 (P) L2
L4 7 DUPLICATE REMOVE L3 (1 DUPLICATE REMOVED)
L5 30193 S (FATTY ACID) (P) AMINO

```
L6           21 S L1 (P) L5
L7           10 DUPLICATE REMOVE L    11 DUPLICATES REMOVED)
L8           10 S L7 NOT L4
L9            2 S L8 (P) SUBSTIT?

=> s spacer (p) (succinic or glu or asp)
L10         640 SPACER (P) (SUCCINIC OR GLU OR ASP)

=> s l10 (p) l3
L11           0 L10 (P) L3

=> s tetradecanoyl (p) l3
L12           0 TETRADECANOYL (P) L3

=> d his

     (FILE 'HOME' ENTERED AT 14:18:05 ON 26 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
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L1          9755 S (GLUCAGON-LIKE PEPTIDE-1) OR (GLUCAGON-LIKE PEPTIDE-2) OR GLP
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L5         30193 S (FATTY ACID) (P) AMINO
L6            21 S L1 (P) L5
L7            10 DUPLICATE REMOVE L6 (11 DUPLICATES REMOVED)
L8            10 S L7 NOT L4
L9             2 S L8 (P) SUBSTIT?
L10          640 S SPACER (P) (SUCCINIC OR GLU OR ASP)
L11            0 S L10 (P) L3
L12            0 S TETRADECANOYL (P) L3

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    68.87      69.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -3.91      -3.91

STN INTERNATIONAL LOGOFF AT 14:26:04 ON 26 JUN 2003
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